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- (71) Applicant (for all designated States except US): SANDOZ AG [CH/CH]; Lichtstrasse 35, CH-4056 Basel (CH).
- (72) Inventors; and
- (75) Inventors/Applicants (for US only): LUDESCHER, Johannes [AT/AT]; Kleinsöll 101, A-6252 Breitenbach (AT). STURM, Hubert [AT/AT]; Edith-Stein-Weg 2, A-6020 Innsbruck (AT). WOLF, Siegfried [AT/AT]; Judenwiese 4a, A-6230 Brixlegg (AT).
- (74) Agent: GRUBB, Philip; Novartis AG, Corporate Intellectual Property, CH-4002 Basel (CH).

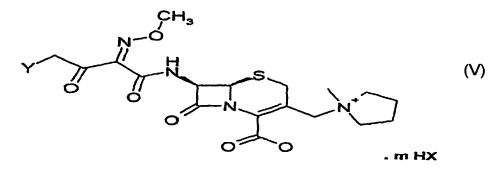
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(54) Title: PROCESSES FOR THE PREPARATIONS OF CEFEPIME



(57) Abstract: This invention provides processes for preparing cefepime, including crystalline intermediates of Formula (V).

Inte ial Application No
PC., \_. 2004/003988

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 C07D501/06 C07D501/44

According to International Patent Classification (IPC) or to both national classification and IPC

#### B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols) IPC 7 C07D

Documentation searched other than minimum documentation to the extent that such documents are included. In the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, BEILSTEIN Data, CHEM ABS Data

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.	
A	EP 0 531 981 A (SQUIBB BRISTOL MYERS CO) 17 March 1993 (1993-03-17) example 31	1-9	
X	US 6 384 215 B1 (DESHPANDE PANDURANG BALWANT ET AL) 7 May 2002 (2002-05-07) column 2, lines 19-24 columns 4-5	1-9	
x	US 2002/156272 A1 (TOTSCHNIG KLAUS ET AL) 24 October 2002 (2002-10-24) inv. 2 page 1, paragraph 5 - paragraph 12 paragraph '0019!	1-4,8,9	
Y	paragraph '0019! page 5, paragraph 46-51 	10-13	

Further documents are listed in the continuation of box C.	X Patent family members are listed in annex.
<ul> <li>Special categories of cited documents:</li> <li>"A" document defining the general state of the art which is not considered to be of particular relevance</li> <li>"E" earlier document but published on or after the international filing date</li> <li>"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)</li> <li>"O" document referring to an oral disclosure, use, exhibition or other means</li> <li>"P" document published prior to the international filing date but later than the priority date claimed</li> </ul>	<ul> <li>"T" later document published after the international filing date or priority date and not in conflict with the application but clied to understand the principle or theory underlying the invention</li> <li>"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone</li> <li>"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.</li> <li>"&amp;" document member of the same patent family</li> </ul>
Date of the actual completion of the international search	Date of mailing of the international search report
21 September 2004	1 4. 10. 2004
Name and mailing address of the ISA  European Patent Office, P.B. 5818 Patentlaan 2  NL - 2280 HV Rijswijk	Authorized officer
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl., Fax: (+31-70) 340-3016	Grassi, D

In inal Application No

Category °	ation) DOCUMENTS CONSIDERED TO BE RELEVANT  Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	EP 0 137 440 A (HOECHST AG) 17 April 1985 (1985-04-17) pages 6-8; claim 1; examples 2-4,10-12,20,21,25,27,44,46,50,53	10-13
X	DATABASE CASREACT XP002297198	14-18
Y	Database accession no. 140:111151 RX(1) & GONG, PING; ZHAO, YANFANG; FENG, RUNLIANG; ZHANG, ZHANTAO: HONGGUO YAOWU HUAXUE ZAZHI, vol. 12, no. 6, 2002, pages 350-351,362,	14-18
Y	US 5 574 154 A (ABU-NASRIEH OMAR) 12 November 1996 (1996-11-12) column 3, lines 36-40; figure 1	14-18
X	WALKER D G: "NEW CEPHALOSPORIN ACYLATING AGENTS DERIVED FROM SYN-2-(2-AMINOTHIAZOL-4-YL)-2-METHOXYIMINO ACETIC ACID. APPLICATION TO THE SYNTHESIS OF CEFEPIME SULFATE" TETRAHEDRON LETTERS, ELSEVIER SCIENCE PUBLISHERS, AMSTERDAM, NL, vol. 31, no. 45, 1990, pages 6481-6484, XP002035970 ISSN: 0040-4039 page 6483	14-18
A	US 4 489 072 A (IMAIZUMI HIROYUKI ET AL) 18 December 1984 (1984-12-18) columns 15-16	1-9

3

national application No. PCT/EP2004/003988

### INTERNATIONAL SEARCH REPORT

Box II Observations where certain claims were found unsearchable (Continuation of Item 2 of first sheet)
This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:
Claims Nos.: because they relate to subject matter not required to be searched by this Authority, namely:
2. Claims Nos.: because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
3. Claims Nos.: because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).
Box III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)
This International Searching Authority found multiple inventions in this international application, as follows:
see additional sheet
1. X As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:
Remark on Protest  The additional search fees were accompanied by the applicant's protest.  X  No protest accompanied the payment of additional search fees.

#### FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. claims: 1-4(part),5-9

Process for the preparation of Cefepime Dihydrochloride Monohydrate starting from compound IIA and the intermediates according to claims 5-9.

2. claims: 1-4(part)

Process for the preparation of Cefepime Dihydrochloride Monohydrate starting from compound IIB.

3. claims: 10-13

Process for the preparation of Cefepime Dihydrochloride. Monohydrate via intermediate VIII.

4. claims: 14-18

Process for the preparation of Cefepime Dihydrochloride Monohydrate applying the reagent XII.

Int Ional Application No PC1/EP2004/003988

_			1017212	
Patent document ited in search report	Publication date		Patent family member(s)	Publication date
P 0531981	A 17-03-1993	AT	209209 T	15-12-2001
., 0501301	. 2, 33 33 3	AU	655838 B2	12-01-1995
		AU	2284492 A	11-03-1993
		BG	61189 B1	28-02-1997
		CA	2077836 A1	11-03-1993
		CN	1070398 A ,B	31-03-1993
		CN	1158333 A ,B	03-09-1997
		CZ	9202780 A3	17-03-1993
		CZ	9600719 A3	11-06-1997
		DE	69232216 D1	03-01-2002 27-06-2002
		DE	69232216 T2 531981 T3	21-05-2002
		DK EG	20184 A	30-09-1997
		EP	0531981 A1	17-03-1993
		ES	2165351 T3	16-03-2002
		FI	924031 A	11-03-1993
		FI	20011921 A	01-10-2001
		ΗŪ	62901 A2	28-06-1993
		IL	103109 A	13-07-1997
		ĴΡ	3434840 B2	11-08-2003
		JP	5194532 A	03-08-1993
		KR	178280 B1	20-03-1999
		MX	9205147 A1	01-03-1993
		NO	923495 A	11-03-1993
		NZ	244295 A	28-08-1995
		OA	9764 A	30-11-1993
		PL	295873 A1	04-05-1993
		PT	531981 T	31-05-2002
		RO	109651 B1	28-04-1995
		SK	33698 A3	12-09-2000
		SK	278092 A3	12-09-2000 27-08-1995
		RU	2042681 C1	14-01-1997
		US Za	5594129 A 9206866 A	09-03-1993
US 6384215	B1 07-05-200	2 NONE		
US 2002156272	A1 24-10-200		411598 B	25-03-2004
		AU	3967000 A	02-11-2000
		MO	0063214 A1	26-10-2000
		EP	1169324 A1	09-01-2002
		US	2002128469 A1	12-09-2002 15-08-2003
		AT	76399 A	25-09-2001
		AT	408225 B 1522000 A	15-02-2001
		AT AT	80099 A	15-04-2004
EP 0137440	A 17-04-198		3409431 A1	18-04-1985
		AU	3388384 A	18-04-1985
		DK	479684 A	09-04-1985
		EP	0137440 A2	17-04-1985
		ES	8603497 A1	16-04-1986
		FI	843933 A	09-04-1985
		GR	80574 A1	01-02-1985 28-11-1985
		HU	37152 A2	28-11-1985 28-11-1986
		1 11 1		
		HU	190878 B	
		HU JP MA	60097983 A 20250 A1	31-05-1985 01-07-1985

Int. al Application No
PUI/EP2004/003988

Patent document cited in search report		Publication date		Patent family member(s)	Publication date
EP 0137440			NO	844006 A	09-04-1985
			PT	79317 A ,B	01-11-1984
			ZA 	8407825 A	29-05-1985
US 5574154	Α	12-11-1996	NONE		
US 4489072	Α	18-12-1984	JP	1404099 C	09-10-1987
			JP	57058689 A	08-04-1982
			JP	62010512 B 1404101 C	06-03-1987 09-10-1987
			JP JP	57082393 A	22-05-1982
			JP	62010995 B	10-03-1987
			JP	1335688 C	11-09-1986
			JP	57099592 A	21-06-1982
			JP	60052755 B	21-11-1985
			AT	378961 B	25-10-1985
			AT AT	55483 A 378962 B	15-03-1985 25-10-1985
			AT	55583 A	15-03-1985
			ÂŤ	378193 B	25-06-1985
			AT	55683 A	15-11-1984
			AT	375082 B	25-06-1984
			AT	410981 A	15-11-1983
			AU	558586 B2	05-02-1987 20-03-1986
			AU Au	4986085 A 568033 B2	20-03-1986 10-12-1987
			AU	4986185 A	20-03-1986
			AU	558649 B2	05-02-1987
			AU	4986285 A	24-04-1986
			AU	558669 B2	05-02-1987
			AU	4986385 A	20-03-1986 20-03-1986
			AU AU	550330 B2 7543881 A	01-04-1982
			BE	890499 A1	25-03-1982
			CA	1204735 A1	20-05-1986
			CA	1200541 A2	11-02-1986
			CH	651837 A5	15-10-1985
			CH CH	652130 A5 652128 A5	31-10-1985 31-10-1985
			CH	652128 A5 652129 A5	31-10-1985
			CS	236493 B2	15-05-1985
			DD	202436 A5	14-09-1983
			DD	208351 A5	02-05-1984
			DE	3137854 A1	15-04-1982
			DE De	3152931 C2 3152932 C2	05-10-1989 08-02-1990
			DE	3152932 C2 3152934 C2	18-01-1990
			DE	3152935 C2	16-07-1992
			DK	421881 A ,B,	15-04-1982
			EG	17373 A	30-12-1990
			ES	8301998 A1	01-04-1983 01-08-1983
			ES ES	8306155 A1 8306156 A1	01-08-1983
			ES	8306157 A1	01-08-1983
			FI	812980 A ,B,	26-03-1982
			FΙ	870153 A ,B,	15-01-1987